Illinois Emergency Management Agency
Instructions for Applicants Requesting Use of
MDS Nordion Yttrium-90 (Y-90) TheraSphere
or SIRTEX Wilmington, LLC Yttrium-90 (Y-90) SIR-Spheres (Rev. 6)

Note: These instructions are for use in the preparation of amendments to medical licenses seeking approval to use MDS Nordion Y-90 TheraSpheres or SIRTEX Wilmington, LLC Y-90 SIR-Spheres. Both products herein referenced to as Y-90 microspheres. If this is a new application, Instructional Set 52.2 and these instructions must be used in the preparation/submittal of a complete application.

(Note: If applicants/licensees wish to perform procedures in addition to or in substitution of those noted below, those procedures must be submitted for review by the Agency.)

1) For an individual to become an authorized user, the individual must meet one of the pathways outlined in Appendix A.

2) The treatment team shall consist of the radiation oncologist (or approved authorized user) and either the medical physicist or radiation safety officer. The treatment team must be physically present during all administration/retrieval procedures. The authorized user must be trained in accordance with 32 Ill. Adm. Code 335.9050 or 335.9100 or the guidelines for interventional radiologists. Training for radiation safety officers and medical physicists should include manufacturer training and meet 32 Ill. Adm. Code 335.9010(f) or 335.9150(d), respectively. All users must submit copies of the agenda and evidence of completion of training for the specific product that is requested. Appendix A contains detailed instructions for documenting training acceptable to the Agency. Technologists participating in these treatments must be accredited by the State of Illinois in nuclear medicine technology or radiation therapy and must also complete the manufacturer's training program.

3) The licensee must commit to all procedures specified in the MDS Nordion Y-90 TheraSphere and the SIRTEX Wilmington, LLC Y-90 SIR-Spheres Instruction Manuals and FDA approved package inserts.

4) For Y-90 microspheres, "prescribed dose" means the total dose (rad or Gy) documented in the written directive. Alternatively, prescribed activity (mCi or GBq) may be used in lieu of prescribed dose. Administration of Y-90 microspheres must be performed in accordance with the written directive. The written directive should include:

   a) Prior to implantation:

      1) The human research subject’s name.

      2) The date.

      3) The signature of an authorized user for Y-90 Microspheres.

      4) The treatment site.

      5) The radionuclide (including the chemical/physical form of [Y-90 microspheres]).
      6) The prescribed dose/activity.

7) If appropriate for the type of microsphere used, the statement "or dose/activity delivered at stasis."

8) The maximum dose(s)/activity(ies) that would be acceptable to the specified site(s) outside the primary treatment site due to shunting (e.g. ling and gastrointestinal tract): and

b) After implantation within 24 hours of completion/termination of the procedure:

1) Total dose/activity delivered to the primary treatment site and to other specified site(s).

2) If the administration was terminated because of stasis, then:

A) The total dose/activity to the treatment site is the value of the total dose/activity administered when the stasis occurred and the administration was terminated.

B) The name of the individual who made the assessment.

C) The date.

D) The signature of an authorized user for Y-90 microspheres.

5) Procedures for administrations requiring a written directive should, for Y-90 microsphere administrations, describe how to quantify the total dose to the treatment site as well as the total dose to other sites upon completion of the administration to confirm that the administration is in accordance with the written directive.

6) The semiannual physical inventory records must be maintained for five (5) years and should include the individual aggregates of the microspheres identifying:

a) The radionuclide and physical form.

b) The unique identification of each vial in which microspheres are contained.

c) The total activity of the aggregate in each vial.

d) The location of each vial.

7) Procedures should describe measures taken to ensure that the bremstrahlung emissions from each patient or human research subject permits her/his release in accordance with 32 Ill. Adm. Code 335.2110.

8) The SSDR safety evaluations for MDS Nordion Y-90 TheraSphere and the SIRTEX Wilmington, LLC Y-90 SIR-Sphere do not cover the use of any other microspheres, including the preparation

of Y-90 on other microspheres by a commercial nuclear pharmacy, the medical use licensee's authorized nuclear pharmacist, or a physician authorized user qualified to prepare radioactive drugs. The medical use of other microspheres will require a new SSD certificate (or safety evaluation by the broad scope medical use licensee) that addresses the conditions of use, safety of the new Y-90 microspheres, and compatibility of the new microspheres with microsphere delivery system(s).

9) The SSDR safety evaluation for a manufacturer's Y-90 microsphere delivery system does not cover the use of any other delivery system with the Y-90 microsphere device. Only the manufacturer's approved TheraSphere Administration Set or SIRTEX SIR-Spheres device shall be used for administration of these products. Before authorization, the medical use of such a delivery system will require a new SSD certificate (or safety evaluation by the broad scope medical use licensee) that addresses the conditions of use, safety of the microsphere delivery system, and compatibility of the new delivery system with the Y-90 microspheres.

10) Since the device/source does not meet the classic definition of "sealed source" in 32 Ill. Adm. Code 310.20, the requirements in 32 Ill. Adm. Code 335 Subpart H and 32 Ill. Adm. Code 340.410 will not apply and no leak testing in the classical sense is required. However, the licensee must commit to the following requirements for this treatment:

a) 32 Ill. Adm. Code 335.30(a) – License Required.

b) 32 Ill. Adm. Code 335.1080 – Report and Notification of a Medical Event.

c) 32 Ill. Adm. Code 335.2010 – Possession, Use, Calibration of Instruments Used to Measure the Activity of Unsealed Radioactive Material.

d) 32 Ill. Adm. Code 335.2030 - Assay of Radiopharmaceutical Dosages.

e) 32 Ill. Adm. Code 335.2060 - Labeling and Use of Vials and Syringes.

f) 32 Ill. Adm. Code 335.2080 and 340.510 - Monitoring for Contamination and Ambient Radiation Dose Rate/Surveys and Monitoring - General. (Note: Licensee must also ensure surveys of equipment/surgical instruments used for implantation/retrieval of the catheter are performed. All surveys must be conducted with instrumentation appropriate for measurement/detection of the radiation associated with Y-90).

g) 32 Ill. Adm. Code 335.2110 – Release of Individuals Containing Unsealed Radioactive Material or Implants Containing Radioactive Material

h) 32 Ill. Adm. Code 335.5020 - Safety Instruction
(Note: This must include instruction for attending staff to pay particular attention to dressings and linen around the catheter for leakage during treatment.)

i) 32 Ill. Adm. Code 335.5030 - Safety Precautions
(Note: Bioassays are not required for administration of Y-90 Microspheres.

j) 32 Ill. Adm. Code 340.540 – Calibration of Survey Instruments.

11) The licensee must monitor all clothing, food services/utensils, bandages and linens used in the patient's room. These items must be treated as contaminated until monitoring indicates otherwise.

12) The Y-90 microsphere dose vial and other disposable equipment used for administering the Y-90 microspheres (including the catheter) should be stored for decay or disposed of as radioactive waste. Any non-disposable items should be stored for decay. Care should be taken to maintain connections and system integrity to avoid potential radioactive contamination. Licensees should re-evaluate their waste disposal program to allow for disposal of the activities/half-life associated with this material.

13) a) The MDS Nordion Y-90 TheraSphere microspheres are currently approved by the U.S. Food and Drug Administration (FDA) under the provisions of a "Humanitarian Device Exemption" (HDE No H9800006), which includes unique restrictions on the medical use of the devices. Nothing in the Agency's license relieves the licensee from complying with those FDA requirements.

b) The SIRTEX Wilmington, LLC Y-90 SIR-Spheres have been approved by the U.S. FDA under a premarket approval application #P990065/S004.

14) An Institutional Review Board is required to approve and monitor the use of the MDS Nordion Y-90 TheraSphere. If this Board determines that the particular use of the Y-90 TheraSphere is for research purposes, the licensee must meet the requirements for research involving human subjects (Note: One of the conditions of approval for an HDE is that there be an Institutional Review Board initial review and approval before a humanitarian use device is used at a facility as well as continuing review of its use).

15) In March 2007 The NRC staff issued an Information Notice IN 2007 10 *Yttrium-90 TheraSphere® and SIRSpheres® Impurities* which is available at http://www.nrc.gov/reading-rm/doc-collections/gen-comm/info notices/2007/in200710.pdf to alert all medical licensees of the presence of radioactive contaminants and possible disposal issues with the two variations of commercially available Y-90 labeled microspheres, TheraSphere® and SIR-Spheres®. Depending on the contaminants, licensees may need to:

a) Hold the remaining microspheres longer in decay-in-storage in accordance with 32 Ill. Adm. Code 340.1045; or

b) Return the microspheres to the manufacturer, if the manufacturer is authorized to receive Y-90 microspheres; or

c) Transfer the microspheres to an authorized recipient.

Appendix A

Pathways to become an authorized user of MDS Nordion Yttrium-90 (Y-90) TheraSphere or SIRTEX Wilmington, LLC Yttrium-90 (Y-90) SIR-Spheres.

a) The authorized user must be trained in accordance with:

1. 32 Ill. Adm. Code 335.9050; and

2. The requirements outlined in subsection (b) of the Guidelines For Interventional Radiologists (below); or

b) 1. 32 Ill. Adm. Code 335.9100; and

2. The requirements outlined in subsection (b) of the Guidelines For Interventional Radiologists (below); or

c) 32 Ill. Adm. Code 335.9160; or

d) The guidelines for Interventional Radiologists (below).

Guidelines For Interventional Radiologists

To authorize an Interventional Radiologist as a user of Y-90 microspheres, the licensee shall require the Interventional Radiologist to be a physician who:

a) Holds an American Board of Radiology certification in diagnostic radiology and subspecialty certification in interventional radiology; or has three years supervised clinical experience in diagnostic radiology and one additional year supervised clinical experience in interventional radiology; and

1) Has 80 hours of classroom and laboratory training for byproduct material, including Y-90 microspheres, which may be concurrent with training received in accordance with Item (a) above in:

A) Radiation physics and instrumentation;

B) Radiation protection;

C) Mathematics pertaining to the use of and measurement of radioactivity;

D) Radiation biology; and

2) Has work experience under the supervision of an authorized user for Y-90 microspheres or a Y-90 microsphere manufacturer representative involving:

A) Ordering, receiving/unpacking radioactive materials safely and performing the related radiation surveys;

B) Performing quality control procedures on instruments used to determine the activity of Y-90 microspheres and performing checks for proper operation of survey meters;

C) Evaluation of each patient or human research subject for the dose/activity of Y-90 microspheres to be administered to each treatment site;

D) Calculating and measuring the activity and safely preparing the Y-90 microspheres to be delivered to the patient or human research subject;

E) Using administrative controls to prevent a medical event involving the use of byproduct material;

F) Using procedures to control and to contain spilled byproduct material, including Y-90 microspheres, safely and using proper decontamination procedures; and

G). Follow up and review of each patient’s or human research subject’s case history for Y-90 microspheres; and

3) The applicant must submit an attestation to training and experience satisfying (a)(1) and (a)(2) from either a representative of the manufacturer of the requested type of microsphere or an authorized user of the requested type of microsphere; and

b) Has successfully completed training in the operation of the delivery system, safety procedures, and clinical use for each type of Y-90 microspheres for which authorization is sought. The additional Y-90 microsphere specific training and experience requirements may be satisfied by satisfactory completion of a training program provided by either:

1) An authorized user who is authorized for the type of microsphere for which the individual is seeking authorization, who has already documented completion of the three supervised clinical cases. The clinical use experience should include at least three supervised hands-on cases for each type of Y-90 microsphere for which the individual is seeking authorized user status; or

2) A Y-90 microsphere manufacturer. The clinical use experience should include at least three supervised hands-on in-vitro simulated cases for each type of Y-90 microsphere for which the individual is seeking authorized user status. In-vitro simulated cases should demonstrate issues that are encountered during Y-90 microsphere administration procedures. Following the license amendment that names the individual as an authorized user for Y-90 microsphere use. The first three patient cases completed by the individual should be hands-on and supervised in the physical presence of a manufacturer representative for each type of Y-90 microsphere for which the individual is authorized; and

3) The applicant must submit documentation for training and experience for:

   A) Individuals obtaining clinical use experience under the above pathway (b)(1) to include:
      1. Attestation to training operation of the requested manufacturer's delivery system
      2. Attestation to training in safety procedures for the use of that type of microsphere
      3. The clinical use cases.

B) Individuals obtaining clinical use experience under the above pathway (b)(2) to include:

1. Completion of the manufacturer's training program, including the in-vitro simulated cases.
2. A commitment that each individual will complete at least the first three hands-on patient cases supervised in the physical presence of a manufacturer representative for each type of Y-90 microsphere for which authorization is sought.
3. The licensee's commitment will also include documentation from the manufacture to the Agency within 30 days of when these three cases have been satisfactorily completed.

AGENCY NOTE: Specialty boards whose certification processes have been recognized by the Agency, the U.S. Nuclear Regulatory Commission or an Agreement State will be posted on NRC's website.

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